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DN

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/610,935	07/06/00	WARD B	

HM12/0404

000321
SENNIGER POWERS LEAVITT AND ROEDEL
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS MO 63102

EXAMINER	
SISSON, B	

ART UNIT	PAPER NUMBER
1645	5

DATE MAILED: 04/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev.11/00)

Office Action Summary	Application No.	Applicant(s)	
	09/610,935	WARD ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-33 is/are pending in the application.

4a) Of the above claim(s) 23-33 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-33 are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1650, Art Unit 1655, and has been assigned to Primary Examiner Bradley L. Sisson.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-22, drawn to a composition suitable for formulation of an enzymatic reaction mixture, classified in class 435, subclass 6.

II. Claims 23-27, drawn to a method for a polymerase reaction, classified in class 435, subclass 91.2.

III. Claims 28-33, drawn to a method for a restriction enzyme reaction, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

3. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process such as the method of Group III.

4. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be sued in a materially different process such as the method of Group II.

5. Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are each drawn to different methods that are comprised of different method steps and result in different end products.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Specification

7. The use of the trademark TWEEN (e.g., TWEEN 20) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-10 are drawn to a "composition suitable for formulation of an enzymatic reaction mixture, the composition comprising a reaction component essential for ex vivo non-polymerase enzymatic reaction." Upon review of the specification, it is noted at page 11, last paragraph, that the "enzyme" may include "those which modify or degrade proteins, lipids, carbohydrates, and metabolites, such as any kinase, protease, lipase, amylase, peroxidase, oxidase, oxygenase, and dehydrogenase. Enzymes which modify, cut, or synthesize nucleic acids are particularly suitable to be used with the present invention. Examples include any ligase, phosphodiesterase, DNase, exonuclease, RNase, phosphatase, kinase, terminal transferase, reverse transcriptase, restriction endonuclease, RNA polymerase, and DNA polymerase."

The specification has been found to set forth but two examples. Example 1, pages 18-30, "Identification and formulation of a Taq DNA polymerase with tracers and high density reagent;" and Example 2, pages 30-31, "Determination of the compatibility of a dye with restriction endonuclease." In Example 1, it is disclosed that"[f]rom 180+ red dyes (absorbance

max between 450 and 570 nm) (Table 1)" but 6 dyes (Bordeaux 1, Acid Red 106, Acid Red 4, Acid Red 1, Amaranth, and Acid Violet 97) have been found to be compatible with Taq polymerase. In Example 2, but one dye was studied (Amaranth) and then with only a few restriction endonucleases. The specification odes not provide an adequate written description of any other dyes that meet the function requirements of claims 1-22, and especially any of the other enzymes encompassed by claims 1-10. While the specification has been found to provide a listing of possible enzymes, the listing of enzymes does not rise to the level of identifying which dye(s) would be suitable for use with any of the myriad of enzymes encompassed by the claims. Clearly, applicant is seeking protection for a vast genus of compositions yet has provided but a few examples of that ~~with~~ which would will be suitable with but one enzyme (Taq) and has evaluated but one dye with a few restriction endonucleases. Such limited disclosure does not satisfy the written description requirement of 35 USC 112, first paragraph. In support of this position, attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.
>
> ***

> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

Attention is also directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

As indicated above, the specification provides a description of but 6 dyes that are suitable with Taq polymerase and but one dye that is suitable with restriction endonucleases. The specification does not identify any other dye that is suitable with any other enzyme. Accordingly, the specification does not reasonably suggest that applicant was in possession of any other compositions at the time of filing. While applicant has disclosed a method that could possibly be used for the identification of other dyes, such a teaching, while possibly being enabling for a method of identification of other dyes suitable for use with either Taq polymerase or restriction endonuclease, does not rise to the level of providing an adequate written description of those compositions which have the required properties. Accordingly, claims 1-22 are rejected under 35 USC 112, first paragraph, as it relates to the failure of the specification to provide an adequate written description of the invention.

10. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance provided and the Presence or Absence of Working Examples

The specification provides but two examples, Example 1, pages 18-30, "Identification and formulation of a Taq DNA polymerase with tracers and high density reagent;" and Example 2, pages 30-31, "Determination of the compatibility of a dye with restriction endonuclease."

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The prior art teaches the addition of dyestuffs subsequent to the performance of an enzyme-catalyzed reaction. However, the art is profoundly limited where dyestuff was present in the reaction mixture at the time the enzyme was used.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have a broad scope, encompassing a broad genus of compositions comprised of any of a large number of enzymes with a dyestuff. It is noted at page 11, last paragraph, that the "enzyme" may include "those which modify or degrade proteins, lipids, carbohydrates, and metabolites, such as any kinase, protease, lipase, amylase, peroxidase, oxidase, oxygenase, and dehydrogenase. Enzymes that modify, cut, or synthesize nucleic acids are particularly suitable to

be used with the present invention. Examples include any ligase, phosphodiesterase, DNase, exonuclease, RNase, phosphatase, kinase, terminal transferase, reverse transcriptase, restriction endonuclease, RNA polymerase, and DNA polymerase."

Other than performing PCR with Taq, the specification is essentially silent as to what conditions were employed when using any of the compositions now claimed. Seemingly, applicant is relying upon those of skill in the art to determine how, if at all, prior art methods are to be modified so as to enable the use of the claimed compositions. Such reliance upon the public, and not the specification for enablement, is an unfair shift in the responsibility for providing full enablement of the claimed compositions. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385,

> 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-22 have not been found to be enabled by the specification.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
April 2, 2001